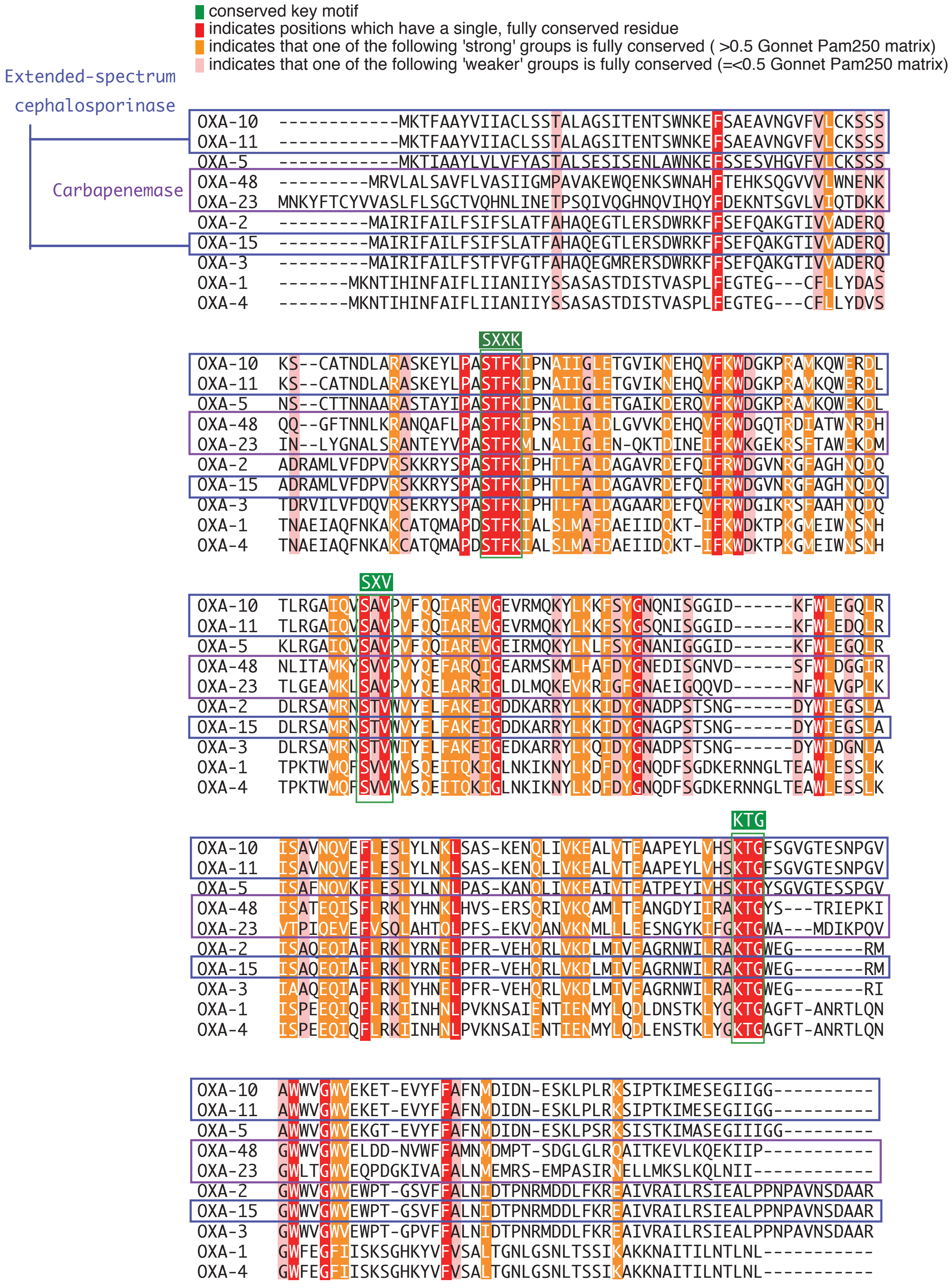

🟩 conserved key motif
🟥 indicates positions which have a single, fully conserved residue
🟧 indicates that one of the following 'strong' groups is fully conserved (>0.5 Gonnet Pam250 matrix)
▨ indicates that one of the following 'weaker' groups is fully conserved (=<0.5 Gonnet Pam250 matrix)

Extended-spectrum cephalosporinase

Carbapenemase

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OXA-10   ------------MKTFAAYVIIACLSSTALAGSITENTSWNKEFSAEAVNGVFVLCKSSS
OXA-11   ------------MKTFAAYVIIACLSSTALAGSITENTSWNKEFSAEAVNGVFVLCKSSS
OXA-5    ------------MKTIAAYLVLVFYASTALSESISENLAWNKEFSSESVHGVFVLCKSSS
OXA-48   ---------MRVLALSAVFLVASIIGMPAVAKEWQENKSWNAHFTEHKSQGVVVLWNENK
OXA-23   MNKYFTCYVVASLFLSGCTVQHLINETPSQIVQGHNQVIHQYFDEKNTSGVLVIQTDKK
OXA-2    ---------MAIRIFAILFSIFSLATFAHAQEGTLERSDWRKFFSEFQAKGTIVVADERQ
OXA-15   ---------MAIRIFAILFSIFSLATFAHAQEGTLERSDWRKFFSEFQAKGTIVVADERQ
OXA-3    ---------MAIRIFAILFSTFVFGTFAHAQEGMRERSDWRKFFSEFQAKGTIVVADERQ
OXA-1    -------MKNTIHINFAIFLIIANIIYSSASASTDISTVASPLFEGTEG---CFLLYDAS
OXA-4    -------MKNTIHINFAIFLIIANIIYSSASASTDISTVASPLFEGTEG---CFLLYDVS

                             SXXK
OXA-10   KS--CATNDLARASKEYLPASTFKIPNAIIGLETGVIKNEHQVFKWDGKPRAMKQWERDL
OXA-11   KS--CATNDLARASKEYLPASTFKIPNAIIGLETGVIKNEHQVFKWDGKPRAMKQWERDL
OXA-5    NS--CTTNNAARASTAYIPASTFKIPNALIGLETGAIKDERQVFKWDGKPRAMKQWEKDL
OXA-48   QQ--GFTNNLKRANQAFLPASTFKIPNSLIALDLGVVKDEHQVFKWDGQTRDIATWNRDH
OXA-23   IN--LYGNALSRANTEYVPASTFKMLNALIGLEN-QKTDINEIFKWKGEKRSFTAWEKDM
OXA-2    ADRAMLVFDPVRSKKRYSPASTFKIPHTLFALDAGAVRDEFQIFRWDGVNRGFAGHNQDQ
OXA-15   ADRAMLVFDPVRSKKRYSPASTFKIPHTLFALDAGAVRDEFQIFRWDGVNRGFAGHNQDQ
OXA-3    TDRVILVFDQVRSEKRYSPASTFKIPHTLFALDAGAARDEFQVFRWDGIKRSFAAHNQDQ
OXA-1    TNAEIAQFNKAKCATQMAPDSTFKIALSLMAFDAEIIDQKT-IFKWDKTPKGMEIWNSNH
OXA-4    TNAEIAQFNKAKCATQMAPDSTFKIALSLMAFDAEIIDQKT-IFKWDKTPKGMEIWNSNH

                 SXV
OXA-10   TLRGAIQVSAVPVFQQIAREVGEVRMQKYLKKFSYGNQNISGGID------KFWLEGQLR
OXA-11   TLRGAIQVSAVPVFQQIAREVGEVRMQKYLKKFSYGSQNISGGID------KFWLEDQLR
OXA-5    KLRGAIQVSAVPVFQQIAREVGEIRMQKYLNLFSYGNANIGGGID------KFWLEGQLR
OXA-48   NLITAMKYSVVPVYQEFARQIGEARMSKMLHAFDYGNEDISGNVD------SFWLDGGIR
OXA-23   TLGEAMKLSAVPVYQELARRIGLDLMQKEVKRIGFGNAEIGQQVD------NFWLVGPLK
OXA-2    DLRSAMRNSTVWVYELFAKEIGDDKARRYLKKIDYGNADPSTSNG------DYWIEGSLA
OXA-15   DLRSAMRNSTVWVYELFAKEIGDDKARRYLKKIDYGNAGPSTSNG------DYWIEGSLA
OXA-3    DLRSAMRNSTVWIYELFAKEIGEDKARRYLKQIDYGNADPSTSNG------DYWIDGNLA
OXA-1    TPKTWMQFSVVWVSQEITQKIGLNKIKNYLKDFDYGNQDFSGDKERNNGLTEAWLESSLK
OXA-4    TPKTWMQFSVVWVSQEITQKIGLNKIKNYLKDFDYGNQDFSGDKERNNGLTEAWLESSLK

                                                    KTG
OXA-10   ISAVNQVEFLESLYLNKLSAS-KENQLIVKEALVTEAAPEYLVHSKTGFSGVGTESNPGV
OXA-11   ISAVNQVEFLESLYLNKLSAS-KENQLIVKEALVTEAAPEYLVHSKTGFSGVGTESNPGV
OXA-5    ISAFNQVKFLESLYLNNLPAS-KANQLIVKEAIVTEATPEYIVHSKTGYSGVGTESSPGV
OXA-48   ISATEQISFLRKLYHNKLHVS-ERSQRIVKQAMLTEANGDYIIRAKTGYS---TRIEPKI
OXA-23   VTPIQEVEFVSQLAHTQLPFS-EKVQANVKNMLLLEESNGYKIFGKTGWA---MDIKPQV
OXA-2    ISAQEQIAFLRKLYRNELPFR-VEHQRLVKDLMIVEAGRNWILRAKTGWEG-------RM
OXA-15   ISAQEQIAFLRKLYRNELPFR-VEHQRLVKDLMIVEAGRNWILRAKTGWEG-------RM
OXA-3    IAAQEQIAFLRKLYHNELPFR-VEHQRLVKDLMIVEAGRNWILRAKTGWEG-------RI
OXA-1    ISPEEQIQFLRKIINHNLPVKNSAIENTIENMYLQDLDNSTKLYGKTGAGFT-ANRTLQN
OXA-4    ISPEEQIQFLRKIINHNLPVKNSAIENTIENMYLQDLENSTKLYGKTGAGFT-ANRTLQN

OXA-10   AWWVGWVEKET-EVYFFAFNMDIDN-ESKLPLRKSIPTKIMESEGIIGG----------
OXA-11   AWWVGWVEKET-EVYFFAFNMDIDN-ESKLPLRKSIPTKIMESEGIIGG----------
OXA-5    AWWVGWVEKGT-EVYFFAFNMDIDN-ESKLPSRKSISTKIMASEGIIIGG---------
OXA-48   GWWVGWVELDD-NVWFFAMNMDMPT-SDGLGLRQAITKEVLKQEKIIP-----------
OXA-23   GWLTGWVEQPDGKIVAFALNMEMRS-EMPASIRNELLMKSLKQLNII------------
OXA-2    GWWVGWVEWPT-GSVFFALNIDTPNRMDDLFKREAIVRAILRSIEALPPNPAVNSDAAR
OXA-15   GWWVGWVEWPT-GSVFFALNIDTPNRMDDLFKREAIVRAILRSIEALPPNPAVNSDAAR
OXA-3    GWWVGWVEWPT-GPVFFALNIDTPNRMDDLFKREAIVRAILRSIEALPPNPAVNSDAAR
OXA-1    GWFEGFIISKSGHKYVFVSALTGNLGSNLTSSIKAKKNAITILNTLNL-----------
OXA-4    GWFEGFIISKSGHKYVFVSALTGNLGSNLTSSIKAKKNAITILNTLNL-----------
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Supplemental Fig. 4. Alignment of the class D β-lactamase OXA family (oxacillinase) OXA-10, OXA-11, and OXA-15 are recognized as extended-spectrum cephalosporinases, whereas OXA-23 and OXA 48 are recognized as CHDLs. Class D β-lactamases retain the tetrad motif S-X-X-K (including the serine of the enzyme active site), the Y-G-N/S triad, and the K-S/T-G triad. Based on the primary sequences, the alignment was generated using Clustal Omega [32, 33, 34] of GenomeNet at Kyoto University Bioinformatics Center (https://www.genome.jp/tools-bin/clustalw).